

Technical aspects of contrast delivery in advanced CT

Patient characteristics, the approach to contrast injection, and the scan itself all influence contrast enhancement.

Kyongtae T. Bae, MD, PhD

Dr. Bae is an Assistant Professor of Radiology at the Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO.

The goal in optimizing contrast delivery is to achieve the greatest contrast enhancement with the least amount of contrast material. No single approach to contrast delivery is effective in all cases, however, as many factors influence contrast enhancement. These factors can be divided into three categories: the patient, the contrast injection, and the scan itself.

Patient factors that influence contrast enhancement include the target organ of interest, the specific diagnostic application, the patient's body size, cardiac output, vascular access, renal function, age, and gender. Factors to consider in contrast injection include the concentration and volume of the contrast material; the rate, pattern, and duration of the injection; and whether or not a saline flush is used. Scanning parameters are also important, particularly the delay between contrast injection and the initiation of scanning, scan duration, whether bolus tracking or some other method is used to adjust for variations in the patient's cardiac output, whether the scan must capture multiple phases of contrast enhancement, and the degree of radiation exposure.

With 16-slice CT, the short duration of scanning makes the timing of image acquisition critical. Faster injection and

higher concentration contrast material can be used to improve contrast enhancement and, perhaps, reduce contrast volume. However, the injection duration and scan delay that are appropriate for a single- or 4-slice CT scan must be recalibrated to optimize contrast enhancement for a 16-slice CT scan.

Injection rate

The effect of injection rate on arterial enhancement is shown in Figure 1. Three time-enhancement curves are created by simulating the injection of contrast material at rates of 1, 3, and 5 mL/sec, while keeping the volume (150 mL) and the concentration (320 mgI/mL) constant. The simulation model is based on an adult man with a body weight of 150 pounds, a height of 5 feet 8 inches, and a normal cardiac output. Two trends are apparent from these time-enhancement curves: As the rate of injection increases, the degree of contrast enhancement increases and the duration of contrast enhancement decreases.

The duration of contrast enhancement is prolonged by slow injection. Prolonged enhancement is preferred with slower CT scanners, to match the long scan duration. It is less critical with fast scanners, however. As a result, fast injection of contrast medium is better suited to multislice CT

angiography (CTA). In addition, fast injection achieves a higher level of arterial enhancement without an increase in contrast volume. Conversely, with fast injection it may be possible to reduce contrast volume and still achieve an acceptable level of contrast enhancement.

There is a limit as to how much contrast volume can be reduced, however. A minimum contrast volume is required for the following reasons. First, patient safety precludes increasing the injection rate indefinitely, as fast injections increase the risk of extravasation and other physiologic complications. Second, contrast enhancement must be sustained at a desirable level over the finite duration of the CT scan. Third, as contrast medium is injected intravenously, it is diluted by the central blood volume before reaching and enhancing the target organ. A sufficient iodine mass must be achieved within the circulatory system to generate a diagnostically useful level of contrast enhancement. The critically required minimum contrast volume for mixing with the central blood reservoir depends on patient size, blood volume, and physiology.

High injection rates are effective for dual-phase CT scanning. Figure 2 shows arterial and hepatic time-enhancement curves simulated with injection rates of

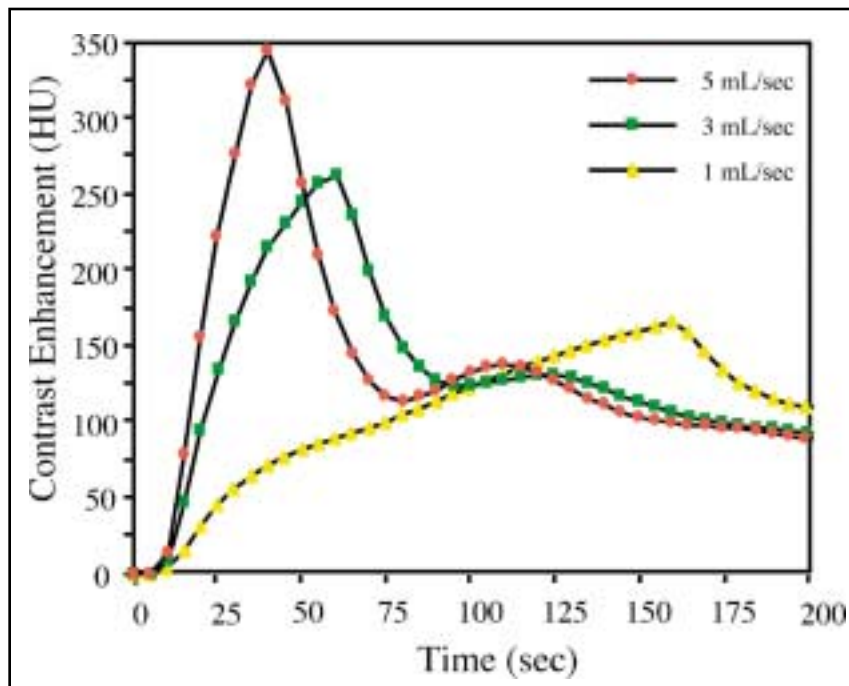


FIGURE 1. Effect of injection rate on arterial contrast enhancement. Simulated aortic time-enhancement curves in which the volume of contrast medium is held constant at 150 mL and the concentration at 320 mgI/mL. As the rate of injection increases, the intensity of contrast enhancement increases and the duration of contrast enhancement decreases.

2 and 5 mL/sec. Compared with slow contrast injection at 2 mL/sec, rapid injection at 5 mL/sec magnifies the difference in the degree of enhancement during the arterial and portal venous phases, and increases the temporal separation between their respective enhancement peaks.

Injection bolus shaping

Bolus shaping is another way to modify contrast delivery. Uniphasic injection is the most common way to administer a bolus of contrast. It involves delivery of contrast material at a constant rate throughout the injection, with a resulting peak in aortic enhancement near the completion of the injection.¹

An alternative approach, biphasic injection, involves a fast injection of contrast material followed by a slow injection. The advantage of the biphasic injection is that it can prolong contrast enhancement. However, neither uniphasic nor biphasic injections achieve the ideal uniform prolonged contrast enhancement.

A third, and perhaps more effective, approach is the exponentially decelerated injection, which involves an exponential decline in the injection rate over time. The exponentially decelerated injection has been tested mathematically and in animals. In a recent human study, we compared two different 40-second injection protocols in the same patients.² The first involved uniphasic contrast injection at a constant rate of 4 mL/sec and the other, exponentially decelerated injection following the formula:

$$4\exp(-0.01t)\text{mL/sec}$$

We found that the exponentially decelerated injection generated uniform contrast enhancement while using less contrast material (134 mL, versus 160 mL with uniphasic injection), although peak enhancement was reduced (Figure 3).

Uniform contrast enhancement is desirable in CTA and cardiac CT, as well as in brain perfusion studies.³ One of the advantages of uniform enhancement is that it becomes less critical to

time image acquisition precisely to correspond to peak contrast enhancement.

Concentration

Figure 4 illustrates the effects of concentration on aortic and hepatic enhancement. Three time-enhancement curves are simulated for the aorta and liver by varying the concentrations of contrast medium (300, 350, and 400 mgI/mL) but keeping the total iodine mass constant (42 g). The volume of contrast medium corresponding to these concentrations is 140, 120, 105 mL, respectively. When the same injection rate of 5 mL/sec is used for all injections, contrast medium with a higher concentration delivers more iodine mass per second, resulting in earlier and greater peak aortic enhancement. Since the contrast volume is reduced with high-concentration contrast material, the duration of enhancement is shorter, but the net effect is an increase in aortic contrast enhancement. The effect of contrast concentration on the liver is not as pronounced as in the aorta.

There are several potential advantages of using high-concentration contrast material. First, we can deliver more iodine without increasing the injection rate. Conversely, the injection rate can be reduced while still achieving the same desired level of enhancement. Improvement in enhancement is evident when 370 mgI/mL contrast material is compared with 300 mgI/mL contrast material. However, the degree of improvement in contrast enhancement with 370 mgI/mL contrast material as compared with 350 mgI/mL contrast material may be marginal. Cost savings are another potential advantage of using high-concentration contrast media, as price generally may vary by volume, not by iodine concentration.

A major disadvantage of high-concentration contrast material is viscosity. The higher the concentration, the more viscous the contrast agent becomes.

Contrast Use in CTA Applications

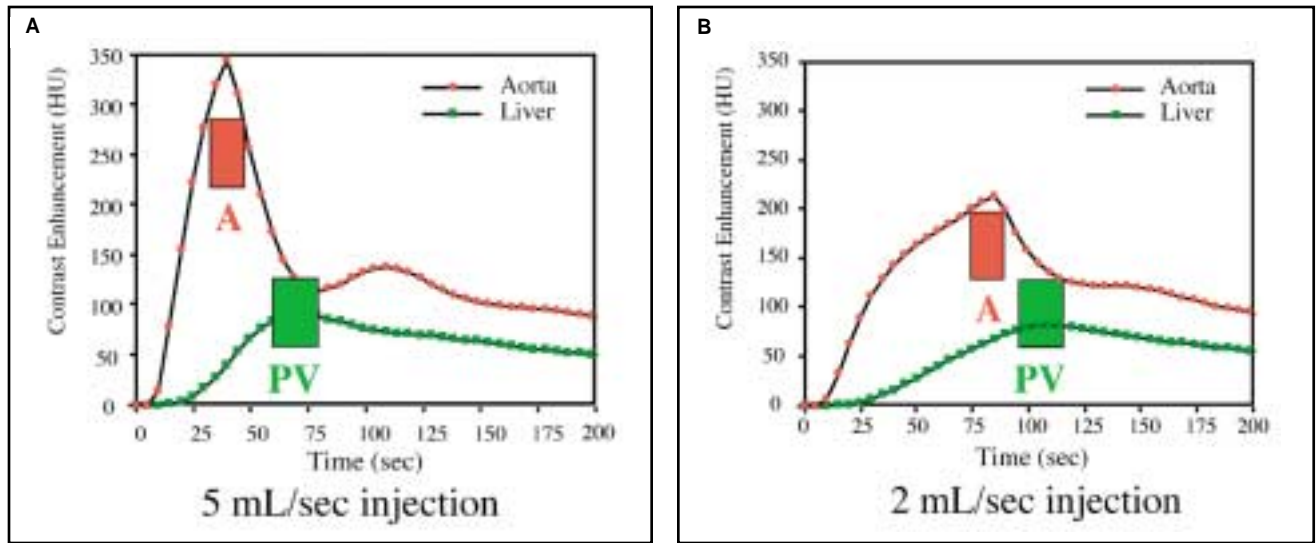


FIGURE 2. Dual-phase scan: (A) Fast (5 mL/sec) versus (B) slow (2 mL/sec) injections. High injection rates are effective for dual-phase scanning of the liver, as they magnify the difference in the degree of enhancement during the arterial (A) and portal venous (PV) phases, and increase the temporal separation between their respective enhancement peaks.

Injection duration

Injection duration may be the most important factor in optimizing contrast delivery in CT. Injection duration critically affects both the degree of contrast enhancement and the timing of peak contrast enhancement and, therefore, optimal scan timing.

The contrast enhancement curves in Figure 5 show the effect on peak aortic enhancement of contrast injections ranging from 1 to 30 seconds in duration.⁴ As the injection duration increases, peak enhancement is delayed and the enhancement curve becomes more asymmetric. With short injections, the timing of peak contrast enhancement depends predominantly on physiological variables, such as cardiac output and circulation course. With long injections, however, the influence of injection duration on the timing of peak contrast enhancement dominates.

The approach to determining injection duration must be adjusted with advances in CT scanner technology. In general, injection duration must be sufficiently long to produce good enhancement. With a shorter scan, a reduced injection duration may be used. But if the injection

duration is too short, contrast volume may not be adequate and contrast enhancement may be suboptimal.

With single- and 4-slice CT scanners, a common approach to determining the injection duration for CTA is to keep the injection duration identical to the scan duration. This approach, however, may no longer work with 16-slice scanners, as scans are much shorter. An injection duration equal to the scan duration may result in poor enhancement. We may increase enhancement by using a higher injection rate, but there are practical restrictions on the degree to which we can increase the injection rate to compensate for a short injection duration or low contrast volume.

One option for estimating injection duration for a short scan is to add a constant factor to the scan duration, for example, 10 seconds. Another approach takes into consideration the patient's physiology and the injection rate. If, for example, achieving a peak aortic enhancement of 200 HU requires 50 mL of contrast material to be injected at 5 mL/sec, the injection duration is 10 seconds. If the duration of the scan itself is 7 seconds and we want to

keep the enhancement above 200 HU throughout the scan, the optimal injection duration for the scan would be 17 seconds. An optimal injection duration for each examination can be determined empirically or perhaps through pharmacokinetic modeling.

In peripheral run-off studies in a subject with normal cardiac output, the transit of contrast medium or blood flow from the abdominal aorta to the ankles typically takes 15 to 20 seconds. In an ideal situation, the CT scan travels with or "chases after" the contrast flow at the same speed and direction, so that imaging coincides with peak enhancement throughout the course of the vessels. Even with 16-slice scanners, however, peripheral run-off studies typically take 20 to 30 seconds. It is therefore necessary to increase injection duration above that required for the ideal case, ie, the minimum required duration, by about 10 seconds. Conversely, with faster CT scanners, scan speed may exceed contrast flow rates and may have to be slowed to match the scan and the propagation of the peak enhancement along the course of the vessels.

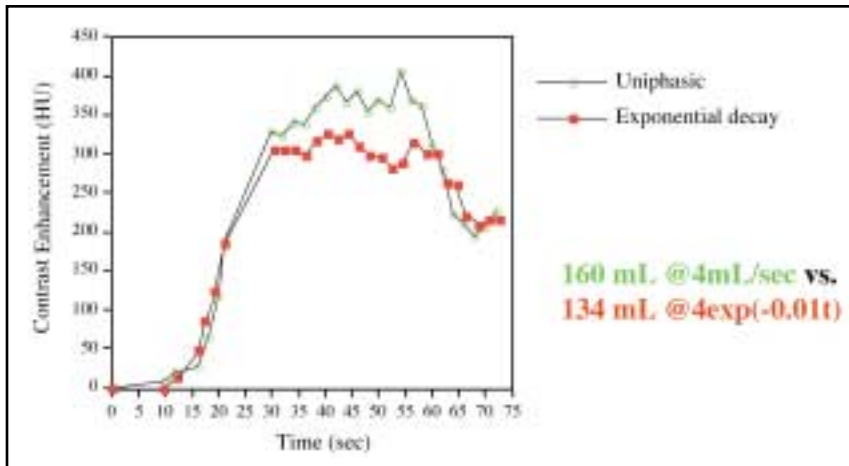


FIGURE 3. Exponentially decelerated injection. Contrast medium administered using the exponentially decelerated injection, as described by the formula $4\exp(-0.01t)$ mL/sec, results in uniform contrast enhancement with less contrast material than a uniphasic injection.

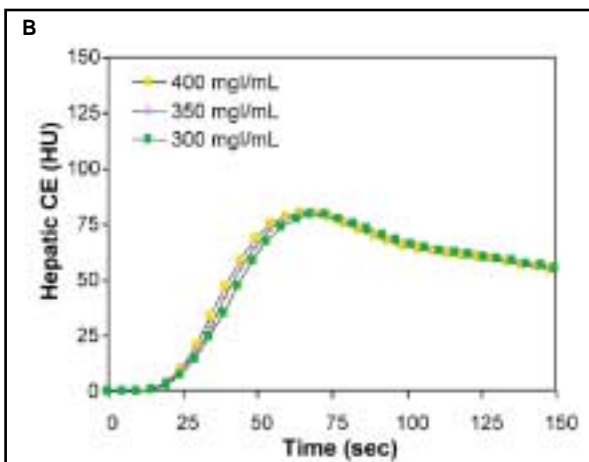
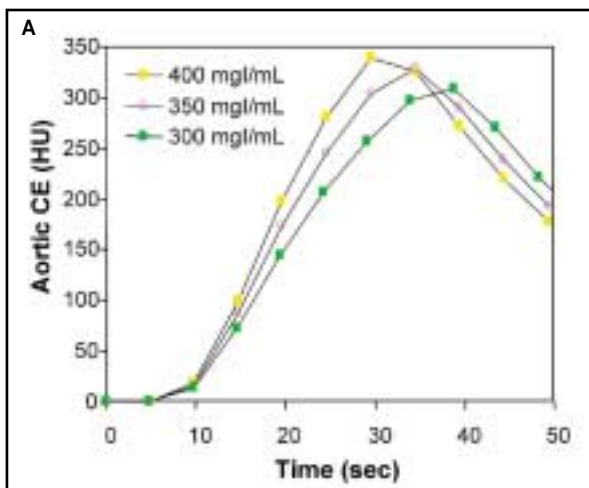


FIGURE 4. (A and B) Effect of high-concentration contrast material on contrast enhancement. Simulated aortic and hepatic time-enhancement curves depict the delivery of a constant iodine mass in a 150-pound man (140 mL of 300 mgI/mL, 120 mL of 130 mgI/mL, and 105 mL of 400 mgI/mL). The use of high-concentration contrast material is associated with earlier and greater peak aortic enhancement. The effect of contrast concentration in the liver (B) is not as pronounced as it is in the aorta (A).

Scan timing

With multislice CT, it is critical to scan during peak contrast enhancement. Three key factors in determining scan timing are cardiac output, injection duration, and scan duration. When cardiac output is reduced, the magnitude of peak enhancement increases (Figure 6), but the times to both contrast arrival and the peak enhancement are delayed.⁵ The delay in time to peak enhancement is approximately the same as that for contrast arrival, and therefore may be predicted by monitoring contrast arrival with a bolus-tracking method.

In determining a scan delay that accounts for variations in cardiac output, a common approach is to use a test bolus of contrast material. A small test bolus is injected and repeat sequential scans are performed at a fixed level to monitor contrast enhancement. For CTA on a single- or 4-slice scanner, the time to peak enhancement of the test bolus is estimated and used to determine the scan delay.

This approach works well for single- and 4-slice scanners, but during a 16-slice scan it may result in scanning too early and completing the study before reaching the peak enhancement. Use of a shorter injection duration with a 16-slice scan can reduce the time to peak enhancement and achieve peak enhancement in the middle of the scan. However, the shortened injection may not provide an adequate degree of enhancement during the scan.

We may, therefore, have to maintain the injection duration for a 16-slice scan at the level used for a single or 4-slice scan. In this case, the scan delay for a 16-slice scan should be longer than for a single or 4-slice scan, ie, estimated from the test-bolus peak enhancement time, to ensure that scanning takes place during the peak contrast enhancement. In an unpublished clinical CTA study with a 16-slice CT scanner, we found that adding approximately 8 seconds to the time of peak test-bolus enhancement corresponded to the

Contrast Use in CTA Applications

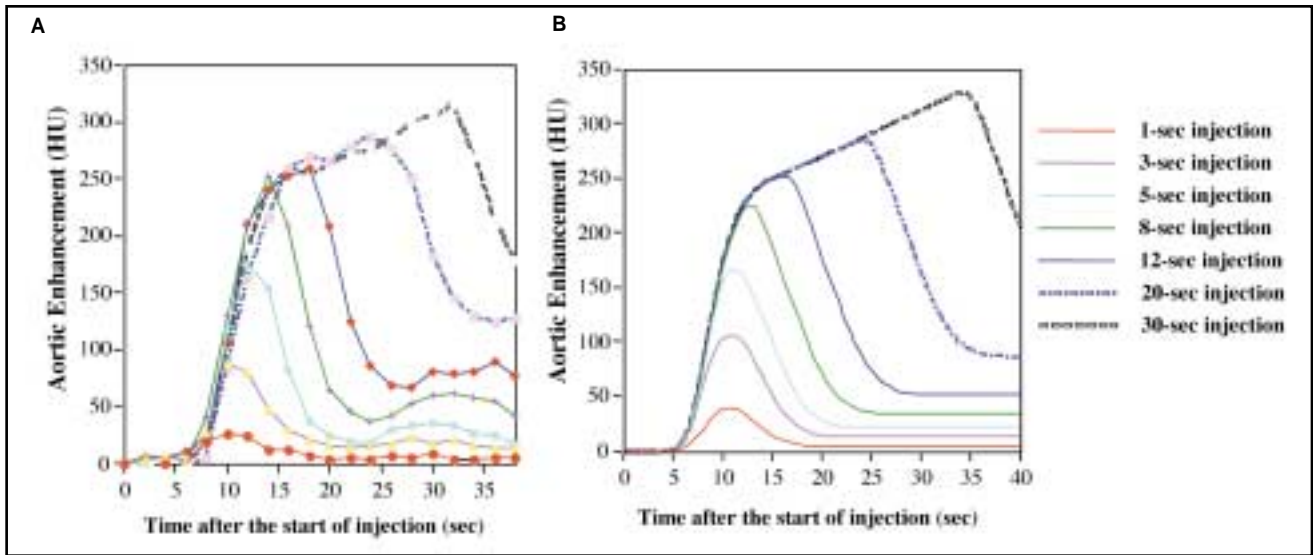


FIGURE 5. Effect of injection duration on peak aortic enhancement: (A) in a porcine experiment and (B) in a simulation. As injection duration increases, peak enhancement is delayed and the enhancement curve becomes more asymmetric. (Figure reprinted with permission from Bae KT. Peak contrast enhancement in CT and MR angiography: When does it occur and why? *Pharmacokinetic study in a porcine model. Radiology. 2003 Jun;227(3):809-816.* Copyright ©2003 Radiological Society of North America.)

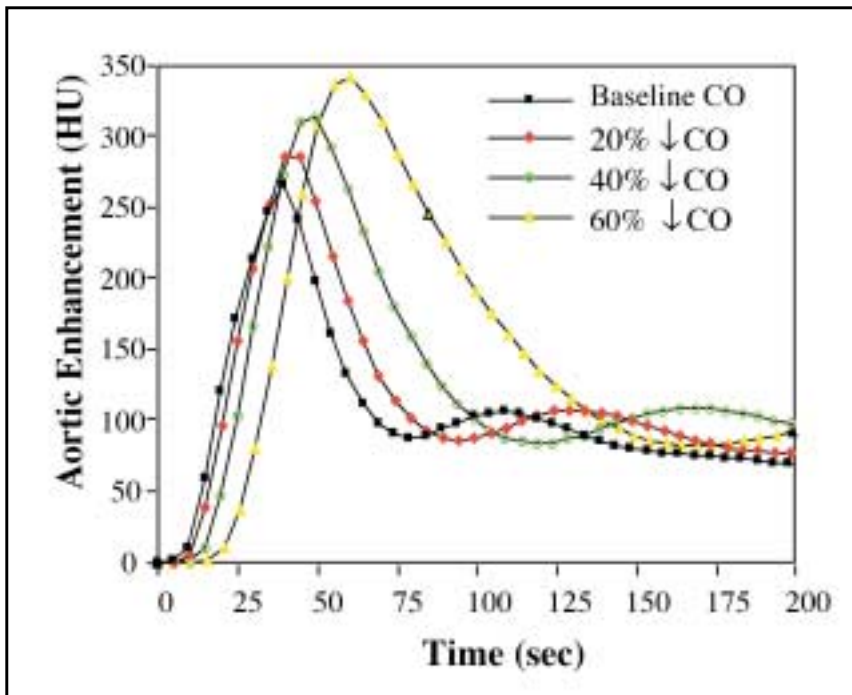


FIGURE 6. Effect of cardiac output on contrast enhancement. Time-enhancement curves simulate the effects of decreasing cardiac output (CO), while holding contrast volume constant at 120 mL and injection rate at 4 mL/sec. When cardiac output is reduced, the magnitude of peak contrast enhancement increases, and the times to contrast arrival and peak enhancement are delayed.

optimal time to begin image acquisition following a full bolus (KT Bae, unpublished data). Nonetheless, this approach is empirical and arbitrary, and its appropriateness with other scan protocols is unknown.

A better approach is to use a bolus-tracking technique, which eliminates the need for a test bolus. Bolus tracking helps to determine contrast arrival and is used to trigger the initiation of scanning. Among the limitations of the bolus-tracking technique, however, is the triggering of the scan by the detection of contrast enhancement above an arbitrary enhancement threshold, which can range from 30 to 150 HU, depending on the operator and CT scanner.

Another limitation of bolus tracking is a delay between the detection of threshold enhancement and the actual initiation of scanning. The delay varies from 2 to 9 seconds, depending on the table position and CT scanner. One solution to compensate for a long delay in image acquisition is to use a low enhancement threshold. In this way, the scan is triggered before the desired enhancement is reached, but image acquisition actually starts at that enhancement level. With 16-slice scanners, short scan times have reduced the

Table 1. Evaluation of pulmonary embolism with 16-slice CT: Determination of optimal scan timing

Scan duration: 10 sec
 120 mL at 4 mL/sec: 30-sec injection
 Contrast arrival (T_{CA}): time at 30–50 HU
 Normal CO: 5 sec
 ↓CO: 20 sec
 Peak time ($T_{PEAK} \approx T_{CA} + T_{ID}$)
 Normal CO: 35 sec
 ↓CO: 50 sec
 Scan timing:
 ($T_{DELAY} = T_{CA} + T_{ID} - (T_{SD} \times 0.75)$)
 Normal CO: 35 – 7 = 28 sec
 ↓CO: 50 – 7 = 43 sec

T_{CA} = contrast arrival time estimated from a bolus-tracking method; CO = cardiac output; T_{ID} = injection duration; T_{SD} = scan duration.

impact of a delay between triggering and image acquisition, making bolus tracking much more practical.

Table 1 illustrates the use of bolus tracking for determining optimal scan timing during an examination for pulmonary embolism. This example assumes a scan duration (T_{SD}) of about 10 seconds. Injection of 120 mL of contrast material at 4 mL/sec results in an injection duration (T_{ID}) of 30 seconds. The contrast arrival time (T_{CA}), defined by a threshold enhancement of 30 HU, would be about 5 seconds for a patient with a normal cardiac output and 20 seconds for a hypothetical patient with low cardiac output. The time to peak contrast enhancement would, therefore, be the sum of the injection duration and the contrast arrival time, or 35 seconds for a patient with normal cardiac output and 50 seconds for a patient with low cardiac output. Scan timing can then be determined by the following formula:

$$T_{CA} + T_{ID} - (T_{SD} \times 0.75).$$

This example demonstrates how a scan delay can be calculated from the scan duration and injection duration, combined with the contrast arrival time measured from the

bolus tracking method, to account for the variations of cardiac output.

Saline flush

The use of a saline flush immediately following contrast injection has several potential advantages. It flushes out contrast material that would otherwise be left behind in the injection tubing. It eliminates the extra step of clearing the vascular access site of residual contrast after injection. By pushing the contrast bolus forward, it may create a more desirable bolus shape. It increases the amount of contrast available for use in image acquisition and may reduce artifact. Typically, a double-barrel power injector is required for a saline flush.

Conclusion

In the future, optimization of contrast delivery may be automated. We will simply swipe an identification card through a card reader to input patient information, specify the organ to be studied, and push a button. Automated protocols will take into account pre-tailored input parameters such as the target organ's ideal level of enhancement, preferred contrast bolus shape, injection rate, concentration, and scan duration. By integrating the patient, injection, and scan factors, the automated program will calculate the optimal injection duration and determine the optimal scan delay in conjunction with bolus tracking technology. During the scan, the contrast injector and the CT scanner will interact, automatically terminating the injection when enough contrast has been delivered.

References

1. Bae KT, Tran HQ, Heiken JP. Multiphasic injection method for uniform prolonged vascular enhancement at CTA: Pharmacokinetic analysis and experimental porcine model. *Radiology*. 2000;216:872-880.
2. Bae KT, Tran HQ, Heiken JP. Uniform vascular contrast enhancement and reduced contrast volume achieved by exponential-decay contrast injection method. *Radiology*. In press.
3. Eastwood JD, Lev MH, Provenzale JM. Perfusion CT with iodinated contrast material. *AJR*

Am J Roentgenol. 2003;180:3-12.

4. Bae KT. Peak contrast enhancement in CTA and MRA: When does it occur and why? *Radiology*. 2003;227:809-816.

5. Bae KT, Heiken JP, Brink JA. Aortic and hepatic contrast enhancement at CT [Part II]: Effect of reduced cardiac output. *Radiology*. 1998;207:657-662.

Discussion

ELLIOT K. FISHMAN, MD:

Thank you very much for a very informative presentation. Does anyone have any questions or comments?

W. DENNIS FOLEY, MD:

I'd like to ask a question. You initially referenced the physiology of the body, particularly intravascular volume and cardiac output. In reference to that, some investigators have proposed weight-based dosing. Could you comment on weight-based dosing, and whether it is an adequate replication of the patient's intravascular volume and cardiac output?

KYONGTAE T. BAE, MD, PhD:

I think so. Certainly, weight is the most important factor in calculating blood volume or even cardiac output in physiology. To determine adequate contrast volume, a weight-based algorithm would be much better than the current fixed injection. You also need to consider other factors. Going back to physiology, for estimating a patient's blood volume, weight is a strong factor; height and gender are also factors, but not as strong.

FOLEY:

I have a follow-up question relating to the use of the bolus-tracking technique, which you are basically marrying to a uniphasic injection.

But you had mentioned the potential use of a biphasic and, then, exponentially decelerated injection techniques. Is the use of a biphasic or exponentially decelerated technique still going to require a preliminary mini-bolus to model? Or can it be used with the bolus-tracking technique?

BAE:

I think bolus tracking can be used. If you are going to use an exponentially decelerated injection, the enhancement curve will go up and then

Contrast Use in CTA Applications

will stay uniform. Peak enhancement timing is not as critical as it is for the single-phase injection, but you still have to know when the contrast arrives. The bolus-tracking method will help you determine that the contrast arrives at the right time.

FISHMAN: You talked about a minimum volume of contrast. How do you define your minimum volume typically?

BAE: That really depends on the patient's weight or size. Last year, at another *Applied Radiology* meeting, Dr. Foley reported that he used 50 mL for CTA of the aorta.

FOLEY: As a rule, 50 to 60 mL is relatively minimum. But even with the 16-channel scanners, you can even go faster than a 10-second acquisition. You can go down to a 5-second acquisition, to do a total abdomen/pelvis. In a patient with marginal renal function, you have two choices. You can stay at 50 to 60 mL, which is probably a reasonable amount of contrast, or you can even go lower. But then the question you raise is that with such a short duration of acquisition, you may not be timing it adequately. But can you compensate for that by, instead of injecting at 5 mL/sec, injecting at 6 or 7 mL/sec? If you're very precise with your acquisition interval, you can still capture a very short duration peak and use a smaller amount of contrast.

BAE: Yes, I think that probably 50 to 60 mL can be minimum for a normal-size patient, approximately 150 pounds, to just capture a certain short segment. But once you scan durations longer than a few seconds, you have to inject more contrast.

FISHMAN: I've seen Dennis' work also, but that was really in select instances where you had questions to answer in small areas. But if I'm studying an abdominal aorta in a patient with reasonable renal function, what would be the minimum contrast you would suggest? In cases of normal BUN creatinine, are there some routine normals that you use?

BAE: Again, it depends on patient size, contrast concentration, and injection rate. While I haven't done a systematic study, in an average-size (150-pound) patient, I would think 70 or 80 mL would be sufficient, if you inject at 5 to 6 mL/sec. But I have little practical experience with injecting low volumes.

FOLEY: I'd like to come back to minimum volume. You suggested that recirculation plays a very important part in increasing aortic enhancement. It requires about 7 seconds into the circulation before you start to see recirculation, and that's fairly constant.

BAE: Yes, it could be in some fast circulatory systems. But, in general, it takes much longer than 7 seconds to see the circulation effect (Figure 5A).

FOLEY: In certain parts of the anatomy, in fact, you want to avoid that recirculation effect, particularly in cerebral work. If you wanted to image the kidneys before you saw the renal vein, which may or may not be an issue, do you want to avoid recirculation, to avoid that second hump of increase of aortic attenuation?

So in other words, for cerebral and for renal studies, instead of trying to delay your acquisition, you may be better off scanning in the early phase, after aortic arrival.

S. JAMES ZINREICH, MD: I have a question: you mentioned saline. In which studies would you apply this technique?

BAE: I cannot speak for the neuro studies, but for cardiac and all other body parts, a saline flush will be very helpful. I think Chris Becker has some slides on that, and he has more experience with that than I do.

DAVID P. NAIDICH, MD: Why would you not use it?

ZINREICH: In the intracranial compartment, obviously, you have this 6-second transit time, and that's what we want to administer the contrast toward. So, in the head, especially the intracranial compartment, it's a shortened time.

SANJAY SAINI, MD: With the flush, though, you grab the tail of the injection; otherwise the tail sort of sits there. Presumably, you use it in every case.

FISHMAN: We decided to use the dual injector also. Of course, we are doing dual-phase imaging, because otherwise you are leaving 8 to 15 mL behind that you are not using, between the line and the peripheral vein. So you're right, there is really no downside for using the saline flush.

I guess in the neuro applications, when you are doing carotids, you are doing a single acquisition; for arterial, it's probably not going to have the impact that it has on the body. So you can potentially lower the volume, even in cranial applications. You could lower the volume of the contrast, probably by 10% or 15%, by making more efficient use of the contrast.

SAINI: Let's say you have two individuals with the same cardiac output, and one has twice the weight of the other individual. Due to the same cardiac output, you would assume that the peak arrival enhancement would be at the same time. But because individual B weighs twice as much, we would want to deliver twice the contrast. So it seems to me you would have to change the injection rate when you give more volume, so that your timing is exactly the same. Something I had not thought about until today was that it seems that if you change the volume, assuming cardiac output is the same, you have to adjust the injection rate.

BAE: I have not thought about putting the weight and the cardiac output together, either. But cardiac output increases with a patient's weight.

FISHMAN: There have been several articles published, and our experience is very similar, that for most patients, you can do preset delays. If I have a 16-slice scanner and I'm doing routine aortic work, why don't I just acquire it 25 sec-

onds arterial, 55 to 60 seconds venous, and not worry about everything. Then I'll go by Mike McCarey—they looked at a range of patients with aortic aneurisms, and it worked fine. We do 30 patients a day, for the most part, using preset delays. In some select patients, you'd be more careful. But is it possible that in the majority of patients you don't need to do that?

BAE: Yes, the majority of patients have close to normal cardiac output, so fixed delays would work. Some people like to use fixed delays, others like to use optimized settings in each individual. Certainly, from the throughput

aspect, fixed delay will work fine. But there will be some patients in whom you are going to miss the bolus.

FISHMAN: For people first getting into CT angiography, I think that this contrast delay always concerns them significantly. So I wonder if we could have rules that say that for this group of patients, you are going to do preset, but in this group of patients you need to do an optimized delay. For instance, in coronary angiography, I would agree that all those patients need some sort of monitoring to determine when to acquire CTA. Or in older patients, in whom it's more difficult.

But if you are doing something as simple as renal donors, or patients under age 50, do you feel comfortable in the simple preset delay? Is there some way we could come up with those rules?

BAE: I think it is a philosophical difference. Really, in every case we do, we use bolus tracking to time it. But I know the other school of thought is to use a fixed delay. Then there will be a few cases for which you miss optimization of contrast. But in the majority of cases, it will be fine with the fixed delay. I don't think that there's a wrong and right answer. But that's the approach I would take.